Barcelona: Autonoma University of Barcelona, 2014, DDD repository <http://ddd.uab.cat/record/123557>

Human-in-the-loop simulation based system for more effective allocation and training of experimenters' groups in stimulation of biotechnological processes

Mieczyslaw Metzger
Faculty of Automatic Control, Electronics and Computer Science, Silesian University of Technology, ul. Akademicka 16, 44-100 Gliwice, POLAND
Email: mieczyslaw.metzger@polsl.pl

Piotr Skupin
Faculty of Automatic Control, Electronics and Computer Science, Silesian University of Technology, ul. Akademicka 16, 44-100 Gliwice, POLAND
Email: piotr.skupin@polsl.pl

***Abstract*—In the case of biotechnological processes, a proper conduction of experiments requires particular attention and skills. This is due to possibilities of causing irreversible damages to living microorganisms when making wrong decisions. In the considered case, two experimenters are enough to conduct a single experiment, but when taking into account the maintenance of process continuity (there is no possibility of stopping the process), then it is necessary to involve more experimenters working in sequentially changing groups. Due to the need to eliminate possible errors, the choice of experimental groups is crucial. In this paper, it is proposed to use human-in-the-loop simulation procedure for selection of experimental groups and for their training before making experiments on real process. For simulation purposes, the process simulator and the collection of processing data were used. This allowed to perform the human-in-the-loop simulations, and then, based on the obtained simulation results, to choose the experimental groups including social conditioning of experimenters.**

I. INTRODUCTION

INCREASING accuracy and precision of available measuring instruments, but also, increasing possibilities and functionalities of supervisory software for experimental, control and monitoring purposes make that the human becomes the weakest link in the whole system.

In the case considered in this paper, the major difficulty is related to the fact that there is a limited number of staff to perform laboratory experiments whose goal is to stimulate the biotechnological process in a proper way. At once, only two experimenters (process operators) can be involved in the performed experiments. The experiments are performed cyclically twenty-four hours a day and include various measurement techniques and procedures. Moreover, the complexity of experiments does not allow all the experimenters to perform all the experiments at same time. Therefore, for the realization of successive experiments on the real and continuous process, it is necessary to choose several working groups (two experimenters in each one), which has to be properly scheduled in the cycle of twenty-four hours a day.

An additional difficulty is the fact that it is not possible to stop the biological process (living biomass / microorganisms) and wrong decisions may essentially (often irreversibly) change biomass parameters. As a result, further supervision and maintenance of the process might be senseless or impossible. Because, social conditioning is also crucial factor, the choice of pairs of experimenters can be supported by the human-in-the loop (HITL) simulation technique. Then, the main criterion for selection of the experimenters' groups is mostly based on the social cooperativity.

The HITL simulations have been used for a long time mainly in the aviation industry for training pilots. However, a key barrier was the cost of simulators that based on expensive computer equipment. The development of cheap microcomputers, and especially, the IT revolution related to the development of small personal computers, has opened the way for the use of HITL simulations for training purposes of industrial process operators (although, it was still expensive), and then, in non-commercial applications (e.g. social and political).

One of the first papers dealing with the problem of supporting a process operator in the chemical or biochemical industry appeared in the last decade of the past century [1]-[4]. An application of the process simulation for the purpose of more efficient operation and process supervision was presented in [1], while the distributed access control schemes [2] were developed to make the operator's training and control easier. In the HITL simulations, colors of elements, which represent industrial plants in the control flow diagrams and the complexity of these diagrams, are crucial [3]. In turn, in the case of emergency situations, it should be possible to perform faster

This work was supported by the National Science Centre under grant No. 2012/05/B/ST7/00096 and by the Ministry of Science and Higher Education under grant BK-UiUA

than real-time simulations [4] (this issue was highlighted in 1994 [4] and it is still under discussion [5]).

At present, the HITL simulation techniques are also used in solving various problems related to social issues. For instance, using methods known from control theory, human behavior in the HITL can be described in similar way as the behavior of PID controller in the closed loop control system [6]. In turn, a framework that provides experimenters and subject matter experts with useful tools to evaluate team performance in terms of task demands was presented in [7]. The HITL simulations are also used to describe human behaviors in emergency situations and in analysis of safety issues, e.g. in the case of fire in automotive manufacturing plants [8]. Another application of the HITL methodology in industry is a decision support system that allows an expert to make appropriate decisions in the case of delivery delays and to analyze risks caused by the unreliable suppliers [9]. Paper by Zenn and Lee [10] proposes the use of HITL approach to describe human-robot-interactions when designing assistive robotic systems. Another interesting example can be found in the paper [11] describing an automobile driving simulator. In order to evaluate characteristics of the human-automobile system, the HITL simulations were applied. Yet other examples are, for instance, HITL for a proper assignment of photos to appropriate groups on social networking Websites [12] or a novel automatic traction control algorithm by incorporating human behavior based on HITL testing. Finally, the paper by Shendarkar and co-workers describes the use of HITL to collect data on human behavior that can be used in crowd evacuation management [14]. In comparison to the existing solutions, the proposed approach in our paper is somewhat novel.

The paper is organized as follows. Section II discusses the problems related to experiments on a biotechnological process and the choice of experimenter groups including their social conditioning. The next section describes the architecture of HITL-based system. Finally, the last section discusses the main results and concluding remarks.

II. PROBLEM UNDER CONSIDERATION

Fig. 1 presents the structure of the system for monitoring, analysis and supervisory control of biotechnological process conducted in a continuously stirred tank bioreactor (CSTB). The main goal of the study is to determine a possible stimulation of the biotechnological process to improve its performance. The CSTB itself is fed with a mixture of several substrates with different inlet concentrations S_1, S_2, …, S_n. In the output stream of the process, a digital microscope camera was mounted to observe the structure of flocks formed by the biomass. Then, for extracting the data from small regions of microscopic images, the Contrast-Limited Adaptive Histogram Equalization (CLAHE) algorithm was used [15].

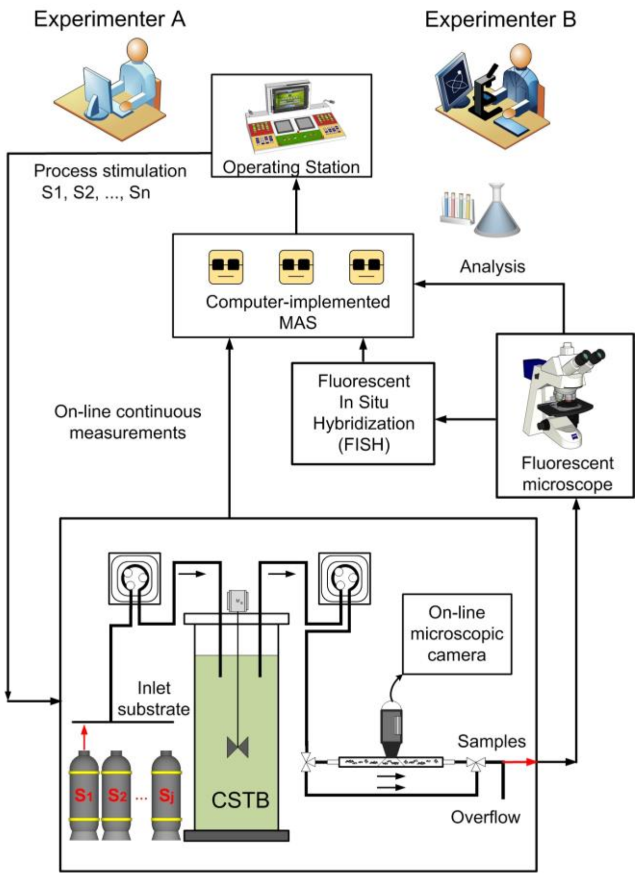

Fig. 1. The general structure of system for monitoring, analysis and control of the continuous flow bioreactor (CSTB) involving two experimenters

Moreover, additional samples of biomass are taken for further analysis including the Fluorescent In-Situ Hybridization (FISH) methods to detect RNA in the cells of microorganisms. Other necessary data (e.g. dissolved oxygen (DO) level, Redox balance or pH values) is provided in real-time by the standard measurement equipment. A multiagent system (MAS) supports the process operator in processing and analysis of the measurement data. More details on the structure and functionality of the MAS can be found in [16], whereas a survey of MAS applications in industrial process control in [17].

Monitoring and control system requires the presence of at least two experimenters (process operators): Experimenter A and Experimenter B. A pair of two experimenters is sufficient to perform necessary chemical and biochemical measurements including FISH analysis. Then, based on the obtained results and the data collected from the on-line measurements, the experimenters can suggest some changes aiming at a more efficient stimulation of the bioprocess. However, the preparation of a schedule of experiments for each experimenter group depends largely on the social conditioning between experimenters. Moreover, due to the presence of living microorganisms in the system, the biological process must be conducted continuously. As a result, the experimenter groups are required to perform their tasks at intervals ranging from four to eight hours depending on the current state of the process. It also means that each group of experimenters must be sufficiently prepared to perform various experiments and, if necessary, to change the stimulation of bioprocess by changing the composition of substrates and/or process parameters.

It should be emphasized that the performed experiments are difficult, laborious and require some expenditure. At the same time, any mistakes made during experiments, accidental omission of experiments and/or wrong decision made by the experimenters may disturb the course of the process and, in extreme cases, cause damage to the culture of microorganisms (biomass). Therefore, it seems obvious to train and instruct all the members from each experimenters' groups (see Fig. 2).

The problem of selection of workgroup members has already been analyzed in the literature, but in the majority of cases, from another point of view than discussed here. For example, the problem of group composition, taking into accounts the preferences of individual group members (i.e. with whom they want to work and cooperate), was presented in [18]. It should be clearly emphasized that in our case, the problem lies in the appropriate allocation of group members (experimenters) from among all the participants of the research project. It means that the composition of working groups cannot be accidental.

Due to above mentioned reasons, the training on a real process is impossible. Furthermore, it is necessary to take into account the behavior of experimenters working in pairs, i.e. their individual preferences (some of them may prefer to work alone and some in a group) and the relations between them. The use of the HITL simulation technique simplifies the incorporation of these factors. Hence, a system for testing and training the experimenter groups has been created. The real bioprocess has been replaced with its simulator and the analysis of the current measurement data has been replaced with the analysis of data from the real experiments.

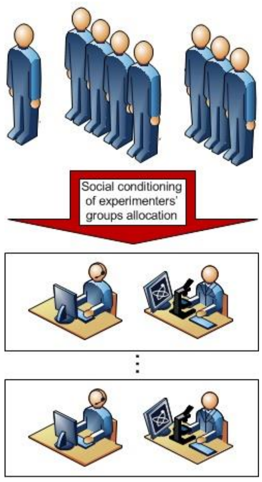

Fig. 2. The allocation of experimenters' groups

III. ARCHITECTURE OF THE HUMAN-IN-THE-LOOP SIMULATION

Fig. 3 presents the architecture of the training system, which is based on the HITL simulations technique. In this case, the HITL simulations use two sources of information: interchangeable bioprocess simulators and samples collected previously from the real experiments. Most of the experiment equipment is the same as in the real bioreactor system. Moreover, for the realization of HITL simulations, the experiment equipment is coupled with the process simulator. Depending on the goal of experiments, it is possible to update or change the structure of the mathematical model of the bioprocess and then to introduce necessary changes to the process simulator.

As shown in Fig. 3, the main feedback loop includes the Experimenter A and the process simulator. The Experimenter B is located in the second loop and, for data analysis training, appropriate measuring samples are chosen and displayed to the experimenter by the process simulator (depending on the current state of the bioprocess). According to the system architecture (Fig.3), both experimenters are located in each of the loops provided that the process simulator can select proper samples for analysis. However, this feedback information is limited to the available collection of samples.

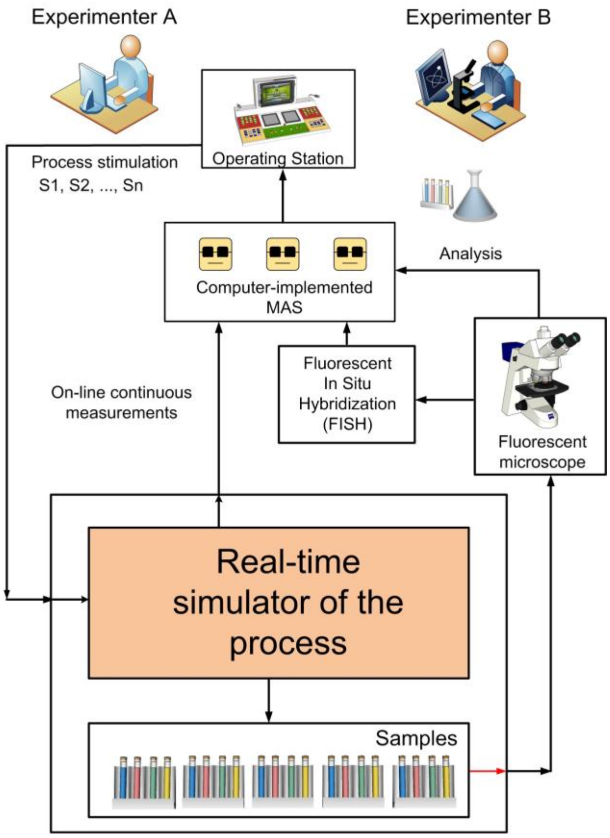

Fig. 3. The system architecture with two feedback loops based on the HITL simulations

If there are no samples that can be selected by the process simulator, then there is no feedback for the Experimenter B in the second loop. Nevertheless, the proposed system can still be useful in training and testing skills of experimenters.

IV. CONCLUDING REMARKS

Based on the HITL simulations, the system for selection and training of the experimenter groups can be very useful before starting the experiments on a real bioprocess. The system allows us to choose the experimenter groups without making expensive and time-consuming experiments, while at the same time incorporating the social conditioning of experimenters. The initial training on the process simulator and the possibility of choosing the pairs of cooperating experimenters can increase the effectiveness of their work when conducting real experiments.

By taking into account the social conditioning, the selection of groups may prove more effective than the classical approach, in which the pairs of cooperating experimenters are usually chosen arbitrarily. In our case, it is of great importance since the experiments are conducted twenty-four hours a day, several days in a row.

The most important social conditionings that were taken into account are: possibility of participation in experiments conducted at night, a distance between the experimenter's home and laboratory, and which are particularly important, the relations between experimenters and their individual preferences for work in a particular group.

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